

30 depression-relevant abstracts

november/december '14 newsletter

(Agudelo, Femenía et al. 2014; Andrade 2014; Böhnke, Lutz et al. 2014; Cotten, Ford et al. 2014; Fels 2014; Fergusson, Horwood et al. 2014; Ford, Quigley et al. 2014; Ivins, Di Simplicio et al. 2014; Jiang, Qin et al. 2014; Keyes, Pratt et al. 2014; Köhler, Benros et al. 2014; Loprinzi and Mahoney 2014; Marazziti, Akiskal et al. 2014; Mrazek, Hornberger et al. 2014; NICE 2014; O'Neil, Berk et al. 2014; O'Neil, Quirk et al. 2014; Okumura and Ichikura 2014; Pompili, Lester et al. 2014; Rosenbaum, Tiedemann et al. 2014; Sala, Goldstein et al. 2014; Sarris, I. Papakostas et al. 2014; Shahmansouri, Farokhnia et al. 2014; Sharpe, Walker et al. 2014; Tsai, Elhai et al. 2014; Van Dam, Hobkirk et al. 2014; Vashum, McEvoy et al. 2014; Walker, Hansen et al. 2014; Walker, Hansen et al. 2014; Wardenaar, Conradi et al. 2014; Wiersma, Van Schaik et al. 2014)

Agudelo, Leandro Z., T. Femenía, et al. (2014). **"Skeletal muscle pgc-1 α 1 modulates kynurenine metabolism and mediates resilience to stress-induced depression."** *Cell* 159(1): 33-45. [http://www.cell.com/cell/abstract/S0092-8674\(14\)01049-6](http://www.cell.com/cell/abstract/S0092-8674(14)01049-6)

Depression is a debilitating condition with a profound impact on quality of life for millions of people worldwide. Physical exercise is used as a treatment strategy for many patients, but the mechanisms that underlie its beneficial effects remain unknown. Here, we describe a mechanism by which skeletal muscle PGC-1 α 1 induced by exercise training changes kynurenine metabolism and protects from stress-induced depression. Activation of the PGC-1 α 1-PPAR α / δ pathway increases skeletal muscle expression of kynurenine aminotransferases, thus enhancing the conversion of kynurenine into kynurenic acid, a metabolite unable to cross the blood-brain barrier. Reducing plasma kynurenine protects the brain from stress-induced changes associated with depression and renders skeletal muscle-specific PGC-1 α 1 transgenic mice resistant to depression induced by chronic mild stress or direct kynurenine administration. This study opens therapeutic avenues for the treatment of depression by targeting the PGC-1 α 1-PPAR axis in skeletal muscle, without the need to cross the blood-brain barrier. (See discussion in Forbes at <http://www.forbes.com/sites/daviddisalvo/2014/10/06/study-exercise-protects-the-brain-against-depression/>).

Andrade, C. (2014). **"Antidepressant augmentation with anti-inflammatory agents."** *J Clin Psychiatry* 75(9): 975-977. <http://www.ncbi.nlm.nih.gov/pubmed/25295422>

Antidepressant augmentation strategies are commonly employed to treat depressed patients who do not respond to antidepressant monotherapy. Neuroinflammatory mechanisms have been implicated in depression, and nonsteroidal anti-inflammatory drugs (NSAIDs) have been found effective in animal models of depression both in monotherapy and when used to augment antidepressant drugs. However, results with NSAIDs have been mixed in human observational studies, with both better and worse depression outcomes reported. Four small (pooled N = 160) randomized controlled trials suggest that celecoxib (200-400 mg/d) augmentation of antidepressant medication improves 4-6 week outcomes in major depressive disorder. There are no data, however, to support the use of celecoxib or other NSAIDs in antidepressant-resistant depression. There are also concerns about adverse events associated with NSAID treatment, and about pharmacodynamic drug interactions between these drugs and serotonin reuptake inhibitors. A reasonable conclusion for the present is that NSAID augmentation of antidepressants is, at best, a tentative approach in nonrefractory major depression.

Böhnke, J. R., W. Lutz, et al. (2014). **"Negative affectivity as a transdiagnostic factor in patients with common mental disorders."** *Journal of Affective Disorders* 166(0): 270-278. <http://www.sciencedirect.com/science/article/pii/S0165032714003115>

Abstract Background Screening and monitoring systems are increasingly used in psychotherapy, but it has been questioned whether outcome measurement using multiple questionnaires is warranted. Arguably, type and number of assessment instruments should be determined by empirical research. This study investigated the latent factor structure of a multi-dimensional outcome measurement strategy used in English services aligned to the Improving Access to Psychological Therapies (IAPT) programme. Methods Factor analyses and structural equation models were performed on 11,939 intake assessments of outpatients accessing an IAPT service between 2008 and 2010. We examined whether three routinely employed instruments (PHQ-9 for depression, GAD-7 for anxiety, WSAS for functional impairment) assess empirically different dimensions. Results The instruments were found to assess mainly one general dimension and only some items of the GAD-7 and WSAS assess unique variance beyond this general dimension. In a structural equation model the disorder-specific factor scores were predicted by patients' diagnostic categories. Limitations Since a large naturalistic data base was used, missing data for diagnoses and scale items were encountered. Diagnoses were obtained with brief case-finding measures rather than structured diagnostic interviews. Conclusion Although the items seem to address mostly one dimension, some variance is due to differences between individuals in anxiety and impairment. While this generally supports multi-dimensional assessment in a primary care population, the clinical upshot of the study is to concentrate attention on transdiagnostic factors as a target for treatment.

Cotten, S. R., G. Ford, et al. (2014). **"Internet use and depression among retired older adults in the united states: A longitudinal analysis."** *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences* 69(5): 763-771. <http://psychsocgerontology.oxfordjournals.org/content/69/5/763.abstract>

Objectives. The purpose of this study is to examine the association between Internet use among retired older adults in the United States and changes in a commonly used predictor of depression (the CES-D). Method. Analyzing data from four waves (2002-2008) of the Health and Retirement Survey, we assess whether an available and commonly used index of a depression state was affected by prior values of the index and Internet use. The sample includes 3,075 respondents observed over 4 waves of data, yielding a total of 12,300 observations. We analyzed the effect on depression of Internet use and past depression in a full sample and a matched sample. We also conducted informal tests for confounders. Finally, we tested a basic mediation model to determine whether Internet use affected depression through its relationship with loneliness and social isolation. Results. Across methods, we found a positive contribution of Internet use to mental well-being of retired older adults in the United States, where Internet use reduced the probability of a depression state by one third. We found no evidence of confounding. Some evidence of mediation was found. Discussion. Our dynamic probit model indicates that for retired older adults in the United States, Internet use was found to reduce the probability of a depressed state by about 33%. Number of people in the household partially mediates this relationship, with the reduction in depression largest for people living alone. This provides some evidence that the mechanism linking Internet use to depression is the remediation of social isolation and loneliness. Encouraging older adults to use the Internet may help decrease isolation and depression.

Fels, A. (2014). **Should we all take a bit of lithium.** *The New York Times*. New York.

THE idea of putting a mind-altering drug in the drinking water is the stuff of sci-fi, terrorist plots and totalitarian governments. Considering the outcry that occurred when putting fluoride in the water was first proposed, one can only imagine the furor that would ensue if such a thing were ever suggested. The debate, however, is moot. It's a done deal. Mother Nature has already put a psychotropic drug in the drinking water, and that drug is lithium. Although this fact has been largely ignored for over half a century, it appears to have important medical implications. Lithium is a naturally occurring element, not a molecule like most medications, and it is present in the United States, depending on the geographic area, at concentrations that can range widely, from undetectable to around .170 milligrams per liter. This amount is less than a thousandth of the minimum daily dose given for bipolar disorders and for depression that doesn't respond to antidepressants. Although it seems strange that the microscopic amounts of lithium found in groundwater could have any substantial medical impact, the more scientists look for such effects, the more they seem to discover. Evidence is slowly accumulating that relatively tiny doses of lithium can have beneficial effects. They appear to decrease suicide rates significantly and may even promote brain health and improve mood.

Fergusson, D. M., L. Horwood, et al. (2014). **"Impact of a major disaster on the mental health of a well-studied cohort."** *JAMA Psychiatry* 71(9): 1025-1031. <http://dx.doi.org/10.1001/jamapsychiatry.2014.652>

Importance There has been growing research into the mental health consequences of major disasters. Few studies have controlled for prospectively assessed mental health. This article describes a natural experiment in which 57% of a well-studied birth cohort was exposed to a major natural disaster (the Canterbury, New Zealand, earthquakes in 2010-2011), with the remainder living outside of the earthquake area.
Objective To examine the relationships between the extent of earthquake exposure and mental health outcomes following the earthquakes—net of adjustment for potentially confounding factors related to personal circumstances, prior mental health, and childhood family background.
Design, Setting, and Participants Data were gathered from the Christchurch Health and Development Study, a 35-year longitudinal study of a birth cohort of New Zealand children (635 males and 630 females). This general community sample included 952 participants with available data on earthquake exposure and mental health outcomes at age 35 years.
Exposures A composite measure of exposure to the events during and subsequent to the 4 major (Richter Scale >6.0) Canterbury earthquakes during the years 2010-2011.
Main Outcomes and Measures DSM-IV symptom criteria for major depression; posttraumatic stress disorder; anxiety disorder; suicidal ideation/attempt; nicotine dependence; alcohol abuse/dependence; and illicit drug abuse/dependence. Outcomes were measured approximately 20 to 24 months after the onset of exposure to the earthquakes and were assessed using DSM-IV diagnostic criteria and measures of subclinical symptoms.
Results After covariate adjustment, cohort members with high levels of exposure to the earthquakes had rates of mental disorder that were 1.4 (95% CI, 1.1-1.7) times higher than those of cohort members not exposed. This increase was due to increases in the rates of major depression; posttraumatic stress disorder; other anxiety disorders; and nicotine dependence. Similar results were found using a measure of subclinical symptoms (incidence rate ratio, 1.4; 95% CI, 1.1-1.6). Estimates of attributable fraction suggested that exposure to the Canterbury earthquakes accounted for 10.8% to 13.3% of the overall rate of mental disorder in the cohort at age 35 years.
Conclusions and Relevance Following extensive control for prospectively measured confounding factors, exposure to the Canterbury earthquakes was associated with a small to moderate increase in the risk for common mental health problems.

Ford, A. C., E. M. Quigley, et al. (2014). **"Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: Systematic review and meta-analysis."** *Am J Gastroenterol* 109(9): 1350-1365. <http://www.ncbi.nlm.nih.gov/pubmed/24935275>

OBJECTIVES: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder. Evidence relating to the treatment of this condition with antidepressants and psychological therapies continues to accumulate. **METHODS:** We performed an updated systematic review and meta-analysis of randomized controlled trials (RCTs). MEDLINE, EMBASE, and the Cochrane Controlled Trials Register were searched (up to December 2013). Trials recruiting adults with IBS, which compared antidepressants with placebo, or psychological therapies with control therapy or "usual management," were eligible. Dichotomous symptom data were pooled to obtain a relative risk (RR) of remaining symptomatic after therapy, with a 95% confidence interval (CI). **RESULTS:** The search strategy identified 3,788 citations. Forty-eight RCTs were eligible for inclusion: thirty-one compared psychological therapies with control therapy or "usual management," sixteen compared antidepressants with placebo, and one compared both psychological therapy and antidepressants with placebo. Ten of the trials of psychological therapies, and four of the RCTs of antidepressants, had been published since our previous meta-analysis. The RR of IBS symptom not improving with antidepressants vs. placebo was 0.67 (95% CI=0.58-0.77), with similar treatment effects for both tricyclic antidepressants and selective serotonin reuptake inhibitors. The RR of symptoms not improving with psychological therapies was 0.68 (95% CI=0.61-0.76). Cognitive behavioral therapy, hypnotherapy, multicomponent psychological therapy, and dynamic psychotherapy were all beneficial. **CONCLUSIONS:** Antidepressants and some psychological therapies are effective treatments for IBS. Despite the considerable number of studies published in the intervening 5 years since we last examined this issue, the overall summary estimates of treatment effect have remained remarkably stable.

Ivins, A., M. Di Simplicio, et al. (2014). **"Mental imagery in bipolar affective disorder versus unipolar depression: Investigating cognitions at times of 'positive' mood."** *Journal of Affective Disorders* 166(0): 234-242. <http://www.sciencedirect.com/science/article/pii/S016503271400295X>

(Free full text available) **Background** Compared to unipolar depression (UD), depressed mood in bipolar disorder (BD) has been associated with amplified negative mental imagery of the future ('flashforwards'). However, imagery characteristics during positive mood remain poorly explored. We hypothesise first, that unlike UD patients, the most significant positive images of BD patients will be 'flashforwards' (rather than past memories). Second, that BD patients will experience more frequent (and more 'powerful') positive imagery as compared to verbal thoughts and third, that behavioural activation scores will be predicted by imagery variables in the BD group. **Methods** BD (n=26) and UD (n=26) patients completed clinical and trait imagery measures followed by an Imagery Interview and a measure of behavioural activation. **Results** Compared to UD, BD patients reported more 'flashforwards' compared to past memories and rated their 'flashforwards' as more vivid, exciting and pleasurable. Only the BD group found positive imagery more 'powerful', (preoccupying, 'real' and compelling) as compared to verbal thoughts. Imagery-associated pleasure predicted levels of drive and reward responsiveness in the BD group. **Limitations** A limitation in the study was the retrospective design. Moreover pathological and non-pathological periods of "positive" mood were not distinguished in the BD sample. **Conclusions** This study reveals BD patients experience positive 'flashforward' imagery in positive mood, with more intense qualities than UD patients. This could contribute to the amplification of emotional states and goal directed behaviour leading into mania, and differentiate BD from UD.

Jiang, M., P. Qin, et al. (2014). **"Comorbidity between depression and asthma via immune-inflammatory pathways: A meta-analysis."** *Journal of Affective Disorders* 166(0): 22-29. <http://www.sciencedirect.com/science/article/pii/S0165032714002110>

Abstract Background Depression is often present in patients with asthma and vice versa. In this review, we aimed to summarize reports on the comorbidity of depression and asthma, and to seek evidence that the biological mechanisms of allergy

may have an important role linking asthma and depression. Method To explore the relationship and pathway underpinning this comorbidity, we reviewed medical articles and undertook a meta-analysis of epidemiological studies on (i) incidence of asthma in patients with depression; (ii) morbidity of depression in patients with asthma; (iii) concentration of cytokines in depressed subjects. Results High level of comorbidity of asthma and depression was consistently demonstrated in 10 studies of patients with asthma and four studies of patients with depression. In search of biological connection of the two illnesses, thirty-eight studies were included for Meta-analyses examining differences in allergy related cytokines between patients with depression and non-depressive subjects. In people with depression, concentration of monocytes related cytokines such as IL-1 (1.56 ng/mL, 95% CI: 0.00–3.12, $p=0.05$) was significantly higher than that in non-depressive control subjects. At the same time, some other inflammatory factors including IL-4 (5.77 pg/mL, 95% CI: 2.34–9.21, $p=0.00010$), IL-6 (1.44 ng/mL, 95% CI: 1.05–1.82, $p<0.00001$) and TNF- α (3.01 ng/mL, 95% CI: 1.76–4.26, $p<0.00001$) were extremely significantly higher in depressed people compared with the controls. There was no significant differences of the T cell related cytokine levels, IFN- γ (–0.16 ng/mL, 95% CI: –0.85–7.73, $p=0.97$), accompanied with IL-10 (0.67 ng/mL, 95% CI: –0.84–2.18, $p=0.38$) between depressive and non-depressive groups. Conclusions The varying levels of certain cytokines play an important role in arousing and remitting asthma and depression. That suggests inflammatory response could be a common pathway adjusting both depression and asthma.

Keyes, K. M., C. Pratt, et al. (2014). **"The burden of loss: Unexpected death of a loved one and psychiatric disorders across the life course in a national study."** *Am J Psychiatry* 171(8): 864-871.
<http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2014.13081132>

OBJECTIVE: Unexpected death of a loved one is common and associated with subsequent elevations in symptoms of multiple forms of psychopathology. Determining whether this experience predicts novel onset of psychiatric disorders and whether these associations vary across the life course has important clinical implications. The authors examined associations of a loved one's unexpected death with first onset of common anxiety, mood, and substance use disorders in a population-based sample. **METHOD:** The relation between unexpected death of a loved one and first onset of lifetime DSM-IV disorders was estimated by using a structured interview of adults in the U.S. general population (analytic sample size=27,534). Models controlled for prior occurrence of any disorder, other traumatic experiences, and demographic variables. **RESULTS:** Unexpected death of a loved one was the most common traumatic experience and most likely to be rated as the respondent's worst, regardless of other traumatic experiences. Increased incidence after unexpected death was observed at nearly every point across the life course for major depressive episode, panic disorder, and posttraumatic stress disorder. Increased incidence was clustered in later adult age groups for manic episode, phobias, alcohol use disorders, and generalized anxiety disorder. **CONCLUSIONS:** The bereavement period is associated with elevated risk for the onset of multiple psychiatric disorders, consistently across the life course and coincident with the experience of the loved one's death. Novel associations between unexpected death and onset of several disorders, including mania, confirm multiple case reports and results of small studies and suggest an important emerging area for clinical research and practice.

Köhler, O., M. E. Benros, et al. (2014). **"Effect of anti-inflammatory treatment on depression, depressive symptoms, and adverse effects: A systematic review and meta-analysis of randomized clinical trials."** *JAMA Psychiatry*.
<http://dx.doi.org/10.1001/jamapsychiatry.2014.1611>

Importance Several studies have reported antidepressant effects of anti-inflammatory treatment; however, the results have been conflicting and detrimental adverse effects may contraindicate the use of anti-inflammatory agents. **Objective** To systematically review the antidepressant and possible adverse effects of anti-inflammatory interventions. **Data Sources** Trials published prior to December, 31, 2013, were identified searching Cochrane Central Register of Controlled Trials, PubMed, EMBASE, PsychINFO, Clinicaltrials.gov, and relevant review articles. **Study Selection** Randomized placebo-controlled trials assessing the efficacy and adverse effects of pharmacologic anti-inflammatory treatment in adults with depressive symptoms, including those who fulfilled the criteria for depression. **Data Extraction and Synthesis** Data were extracted by 2 independent reviewers. Pooled standard mean difference (SMD) and odds ratios (ORs) were calculated. **Main Outcomes and Measures** Depression scores after treatment and adverse effects. **Results** Ten publications reporting on 14 trials (6262 participants) were included: 10 trials evaluated the use of nonsteroidal anti-inflammatory drugs (NSAIDs) ($n = 4258$) and 4 investigated cytokine inhibitors ($n = 2004$). The pooled effect estimate suggested that anti-inflammatory treatment reduced depressive symptoms (SMD, –0.34; 95% CI, –0.57 to –0.11; $I^2 = 90\%$) compared with placebo. This effect was observed in studies including patients with depression (SMD, –0.54; 95% CI, –1.08 to –0.01; $I^2 = 68\%$) and depressive symptoms (SMD, –0.27; 95% CI, –0.53 to –0.01; $I^2 = 68\%$). The heterogeneity of the studies was not explained by differences in inclusion of clinical depression vs depressive symptoms or use of NSAIDs vs cytokine inhibitors. Subanalyses emphasized the antidepressant properties of the selective cyclooxygenase 2 inhibitor celecoxib (SMD, –0.29; 95% CI, –0.49 to –0.08; $I^2 = 73\%$) on remission (OR, 7.89; 95% CI, 2.94 to 21.17; $I^2 = 0\%$) and response (OR, 6.59; 95% CI, 2.24 to 19.42; $I^2 = 0\%$). Among the 6 studies reporting on adverse effects, we found no evidence of an increased number of gastrointestinal or cardiovascular events after 6 weeks or infections after 12 weeks of anti-inflammatory treatment compared with placebo. All trials were associated with a high risk of bias owing to potentially compromised internal validity. **Conclusions and Relevance** Our analysis suggests that anti-inflammatory treatment, in particular celecoxib, decreases depressive symptoms without increased risks of adverse effects. However, a high risk of bias and high heterogeneity made the mean estimate uncertain. This study supports a proof-of-concept concerning the use of anti-inflammatory treatment in depression. Identification of subgroups that could benefit from such treatment might be warranted.

Loprinzi, P. D. and S. Mahoney (2014). **"Concurrent occurrence of multiple positive lifestyle behaviors and depression among adults in the united states."** *Journal of Affective Disorders* 165(0): 126-130.
<http://www.sciencedirect.com/science/article/pii/S0165032714002675>

Abstract Background To our knowledge, no studies have examined the dose-response association between concurrent occurrence of multiple positive health behaviors and depression. As a result, the purpose of this study was to examine the dose-response association between concurrent occurrence of lifestyle behaviors (i.e., diet, physical activity, and smoking) on depression symptoms among a national sample of U.S. adults (20–85 yr). **Methods:** Using data from the 2005–2006 NHANES ($n=2574$), diet was assessed from the healthy eating index variable; physical activity was assessed via accelerometry; smoking was assessed from cotinine levels; and depression was assessed from the Patient Health Questionnaire 9 (PHQ-9). **Results:** Each lifestyle behavior was independently associated with depression in the expected direction, and there was also evidence of a dose-response relationship. Compared to those having 0 positive lifestyle factors, those with 1, 2, and 3 positive lifestyle factors, respectively, were 15% ($p=0.38$), 67% ($p=0.001$), and 82% ($p=0.01$) less likely to be classified as having moderate or greater depression symptoms ($PHQ-9 \geq 10$). **Limitations:** The main limitation of this study was the cross-sectional design. **Conclusion:** there is a dose-response relationship between concurrent occurrence of positive lifestyle behaviors and depression symptoms.

Marazziti, D., H. S. Akiskal, et al. (2014). **"Dimorphic changes of some features of loving relationships during long-term use of antidepressants in depressed outpatients."** *Journal of Affective Disorders* 166(0): 151-155. <http://www.sciencedirect.com/science/article/pii/S0165032714002377>

The present study aimed at investigating the possible changes of some features of loving relationships during long-term treatment of depression with both selective serotonin reuptake inhibitors (SSRIs) and tricyclics (TCAs), by means of a specifically designed test, the so-called "Sex, Attachment, Love" (SALT) questionnaire. The sample was composed by 192 outpatients (123 women and 69 men, mean age±SD: 41.2±10.2 years), suffering from mild or moderate depression, according to DSM-IV-TR criteria, that were selected if they were treated with one antidepressant only for at least six months and were involved in a loving relationship. The results showed that SSRIs had a significant impact on the feelings of love and attachment towards the partner especially in men, while women taking TCAs complained of more sexual side effects than men. These data were supported also by the detection of a significant interaction between drug and sex on the "Love" and "Sex" domains. The present findings, while demonstrating a dimorphic effect of antidepressants on some component of loving relationships, need to be deepened in future studies.

Mrazek, D. A., J. C. Hornberger, et al. (2014). **"A review of the clinical, economic, and societal burden of treatment-resistant depression: 1996–2013."** *Psychiatric Services* 65(8): 977-987. <http://ps.psychiatryonline.org/doi/abs/10.1176/appi.ps.201300059>

Treatment-resistant depression exacts a heavy price in treatment costs and lost productivity, reaching into the tens of billions of dollars, but its effects on the lives of patients are just as devastating. In this literature review, the authors summarize 62 studies documenting the disease's toll on quality of life, personal financial resources, and general health. The average patient in the included studies had experienced nearly four earlier episodes of depression, had not responded to 4.7 drug trials, and continued to meet or nearly meet criteria for severe depression. Objective: This literature review assessed the burden of treatment-resistant depression in the United States by compiling published data about the clinical, societal, and economic outcomes associated with failure to respond to one or more adequate trials of drug therapy. Methods: PubMed and the Tufts Cost-Effectiveness Analyses Registry were searched for English-language articles published between January 1996 and August 2013 that collected primary data about treatment-resistant depression. Two researchers independently assessed study quality and extracted data. Results: Sixty-two articles were included (N=59,462 patients). Patients with treatment-resistant depression had 3.8±2.1 prior depressive episodes and illness duration of 4.4±3.3 years and had completed 4.7±2.7 unsuccessful drug trials involving 2.1±.3 drug classes. Response rates for treatment-resistant depression were 36%±1%. A total of 17%±6% of patients had prior suicide attempts (1.1±.2 attempts per patient). Quality-of-life scores (scale of 0–1, with 0 indicating death and 1 indicating perfect health) for patients with treatment-resistant depression were .41±.8 and .26±.8 points lower, respectively, than for patients who experienced remission or response. Annual costs for health care and lost productivity were \$5,481 and \$4,048 higher, respectively, for patients with treatment-resistant versus treatment-responsive depression. Conclusions: Treatment-resistant depression exacts a substantial toll on patients' quality of life. At current rates of 12%–20% among all depressed patients, treatment-resistant depression may present an annual added societal cost of \$29–\$48 billion, pushing up the total societal costs of major depression by as much as \$106–\$118 billion. These findings underscore the need for research on the mechanisms of depression, new therapeutic targets, existing and new treatment combinations, and tests to improve the efficacy of and adherence to treatments for treatment-resistant depression.

NICE (2014). ***Bipolar disorder: The assessment and management of bipolar disorder in adults, children and young people in primary and secondary care***, National Institute for Health And Care Excellence.

(Free full text available) This guideline updates and replaces NICE clinical guideline 38 (published July 2006). It offers evidence based advice on the care and treatment of children, young people and adults with bipolar disorder. Bipolar disorder is a potentially lifelong and disabling condition characterised by episodes of mania (abnormally elevated mood or irritability and related symptoms with severe functional impairment or psychotic symptoms for 7 days or more) or hypomania (abnormally elevated mood or irritability and related symptoms with decreased or increased function for 4 days or more) and episodes of depressed mood. It is often comorbid with other disorders such as anxiety disorders, substance misuse, personality disorders and attention deficit hyperactivity disorder (ADHD). The peak age of onset is 15–19 years, and there is often a substantial delay between onset and first contact with mental health services. The lifetime prevalence of bipolar I disorder (mania and depression) is estimated at 1% of the adult population, and bipolar II disorder (hypomania and depression) affects approximately 0.4% of adults. Bipolar disorder in children under 12 years is very rare. Since the publication of the previous guideline (NICE clinical guideline 38) in 2006, there have been some important advances in our knowledge of the care pathway and treatment approaches that are most likely to benefit people with bipolar disorder. All areas of NICE clinical guideline 38 have been updated. This guideline covers the recognition, assessment and management of bipolar disorder in children, young people and adults. It includes specific recommendations for diagnosis in children and young people because presentation in these age groups can be complicated by other conditions such as ADHD. The recommendations apply to people with bipolar I, bipolar II, mixed affective and rapid cycling disorders. Non-bipolar affective disorders are not covered because these are addressed by other guidelines, and this guideline does not make specific recommendations about other mental disorders that commonly coexist with bipolar disorder.

O'Neil, A., M. Berk, et al. (2014). **"The association between poor dental health and depression: Findings from a large-scale, population-based study (the nhanes study)."** *Gen Hosp Psychiatry* 36(3): 266-270. <http://www.ncbi.nlm.nih.gov/pubmed/24636212>

OBJECTIVE: To examine the relationship of poor dental health and depression, controlling for markers of inflammation (C-reactive protein; CRP) and adiposity (body mass index; BMI). METHOD: Data from two National Health and Nutrition Examination Surveys (2005-2008) were utilized (n=10214). Dental health was assessed using the Oral Health Questionnaire (OHQ). Depression was measured using the Patient Health Questionnaire-9 (PHQ-9), where cases were identified using a cut off score of 10 or above. Logistic regression was applied to measure magnitude of associations, controlling for a range of covariates including CRP and BMI. RESULTS: After adjustment for covariates, a significant dose-response relationship between number of oral health conditions and likelihood of PHQ-9 defined depression was observed. Compared with individuals without an oral health condition, adjusted odds ratio (95% confidence interval) for depression in those with two, four and six conditions were 1.60 (1.08-2.38), 2.13 (1.46-3.11) and 3.94 (2.72-5.72), respectively. Level of CRP and being underweight or obese were associated with being depressed. CONCLUSIONS: A positive association exists between poor dental health and depression that is independent of CRP and BMI.

O'Neil, A., S. E. Quirk, et al. (2014). **"Relationship between diet and mental health in children and adolescents: A systematic review."** *Am J Public Health* 104(10): e31-42. <http://www.ncbi.nlm.nih.gov/pubmed/25208008>

(Available in free full text) We systematically reviewed 12 epidemiological studies to determine whether an association exists between diet quality and patterns and mental health in children and adolescents; 9 explored the relationship using diet as the exposure, and 3 used mental health as the exposure. We found evidence of a significant, cross-sectional relationship between unhealthy dietary patterns and poorer mental health in children and adolescents. We observed a consistent trend for the relationship between good-quality diet and better mental health and some evidence for the reverse. When including only the 7 studies deemed to be of high methodological quality, all but 1 of these trends remained. Findings highlight the potential importance of the relationship between dietary patterns or quality and mental health early in the life span.

Okumura, Y. and K. Ichikura (2014). **"Efficacy and acceptability of group cognitive behavioral therapy for depression: A systematic review and meta-analysis."** *Journal of Affective Disorders* 164(0): 155-164. <http://www.sciencedirect.com/science/article/pii/S0165032714002079>

Abstract Background Despite treatment guidelines for depression placing group cognitive behavioral therapy (group CBT) between low- and high-intensity evidence-based psychological interventions, the validity of the placement remains unknown. We aimed to systematically review evidence for the efficacy and acceptability of group CBT in patients with depression compared to four intensity levels of psychosocial interventions. Methods We searched the Cochrane Central Register of Controlled Trials, MEDLINE, PsycINFO, and Web of Science and hand-searched the references in identified publications. We selected randomized controlled trials comparing group CBT with four levels of interventions for adult patients with depression. Two authors independently assessed risk of bias. Results From 7953 records, we identified 35 studies that compared group CBT to non-active (k=30), low-intensity (k=2), middle-intensity (k=8), and high-intensity (k=1) interventions. Group CBT had a superior efficacy (standardized mean difference [SMD]=-0.68) and a similar acceptability compared to non-active controls. Pooled results showed a small but non-significant excess of group CBT relative to middle-intensity interventions (SMD=-0.21). Limitations Over 60% of studies did not report enough information to judge selection and selective reporting bias. Conclusions These results suggest the need for high-quality trials of group CBT compared to low- and high-intensity interventions.

Pompili, M., D. Lester, et al. (2014). **"Bisexuality and suicide: A systematic review of the current literature."** *The Journal of Sexual Medicine* 11(8): 1903-1913. <http://dx.doi.org/10.1111/jsm.12581>

Introduction Many studies of lesbian, gay, and bisexual youth have demonstrated that individuals reporting a bisexual orientation have a particularly high risk of suicidal behavior and substance abuse. It has been also suggested that bisexual individuals (both men and women) have higher rates of depression and anxiety compared with homosexual and heterosexual groups. Aim The aim of the present article was to determine whether or not an association between bisexuality and suicidal behavior exists and to analyze risk factors for suicidal behavior in bisexual individuals. Main Outcome Measures The combined search strategies yielded a total of 339 records screened from PubMed, Scopus, and Web of Knowledge. Duplicate articles, articles that were not in English, and those that did not analyze bisexuality separately from homosexuality were excluded. A quality assessment was performed for each study included. Methods A careful systematic review of the literature was conducted investigating the potential bisexuality-suicidal behavior link. A total of 77 articles from peer-reviewed journals were considered, and the most relevant (N = 19) were selected for this review. Results Individuals reporting a bisexual orientation had an increased risk of suicide attempts and ideation compared with their homosexual and heterosexual peers. Risk factors included related victimization, peer judgments, and family rejection. Bisexual individuals also reported higher rates of mental illness and substance abuse. Conclusions Bisexual individuals may experience more psychological distress and mental health problems than individuals who identify with a homosexual or heterosexual orientation. Clinicians should consider the potential for suicidal behaviors in bisexual individuals and be alert for increased mental health problems and poor social integration.

Rosenbaum, S., A. Tiedemann, et al. (2014). **"Physical activity interventions for people with mental illness: A systematic review and meta-analysis."** *J Clin Psychiatry* 75(9): 964-974. <http://www.ncbi.nlm.nih.gov/pubmed/24813261>

OBJECTIVE: To determine effects of physical activity on depressive symptoms (primary objective), symptoms of schizophrenia, anthropometric measures, aerobic capacity, and quality of life (secondary objectives) in people with mental illness and explore between-study heterogeneity. **DATA SOURCES:** MEDLINE, Cochrane Controlled Trials Register, PsycINFO, CINAHL, Embase, and the Physiotherapy Evidence Database (PEDro) were searched from earliest record to 2013. **STUDY SELECTION:** Randomized controlled trials of adults with a DSM-IV-TR, ICD-10, or clinician-confirmed diagnosis of a mental illness other than dysthymia or eating disorders were selected. Interventions included exercise programs, exercise counseling, lifestyle interventions, tai chi, or physical yoga. Study methodological quality and intervention compliance with American College of Sports Medicine (ACSM) guidelines were also assessed. **DATA EXTRACTION AND ANALYSIS:** Two investigators extracted data. Data were pooled using random-effects meta-analysis. Meta-regression was used to examine sources of between-study heterogeneity. **RESULTS:** Thirty-nine eligible trials were identified. The primary meta-analysis found a large effect of physical activity on depressive symptoms (n = 20; standardized mean difference (SMD) = 0.80). The effect size in trial interventions that met ACSM guidelines for aerobic exercise did not differ significantly from those that did not meet these guidelines. The effect for trials with higher methodological quality was smaller than that observed for trials with lower methodological quality (SMD = 0.39 vs 1.35); however, the difference was not statistically significant. A large effect was found for schizophrenia symptoms (SMD = 1.0), a small effect was found for anthropometry (SMD = 0.24), and moderate effects were found for aerobic capacity (SMD = 0.63) and quality of life (SMD = 0.64). **CONCLUSIONS:** Physical activity reduced depressive symptoms in people with mental illness. Larger effects were seen in studies of poorer methodological quality. Physical activity reduced symptoms of schizophrenia and improved anthropometric measures, aerobic capacity, and quality of life among people with mental illness.

Sala, R., B. I. Goldstein, et al. (2014). **"Childhood maltreatment and the course of bipolar disorders among adults: Epidemiologic evidence of dose-response effects."** *Journal of Affective Disorders* 165(0): 74-80. <http://www.sciencedirect.com/science/article/pii/S0165032714002298>

Background Childhood maltreatment (CM) is highly prevalent among individuals with bipolar disorders (BP); however few studies have examined its potential role in the course and outcome of individuals with BP. We aim to examine the dose response relationship between the number of types of CM and the course of individuals with BP. Methods As part of the National Epidemiologic Survey on Alcohol and Related Conditions, 1600 adults who met lifetime DSM-IV criteria for BP-I (n=1172) and BP-II (n=428) were included. Individuals were evaluated using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DMS-IV Version and data was analyzed lifetime and from Waves 1 and 2, approximately 3 years apart. Results Around half of individuals with BP had a history of at least one type of CM. Overall, there was a clear dose-response relationship between number of CM and severity of BP across several domains, including clinical characteristics, probability of treatment, lifetime prevalence of psychiatric comorbidity, incidence of anxiety disorders, substance use disorder, and nicotine dependence, and level of psychosocial functioning. Limitations The interviews were conducted by lay professional interviewers rather than clinicians, use of retrospective report to determine CM in individuals with BP, and not all respondents from Wave 1 were able to be interviewed in Wave 2. Conclusions The number of types of CM confers developmental differences in the course of BP with a

worse course and outcome of BP. Early identification and treatment of CM are warranted to improve the course and outcome of individuals with BP.

Sarris, J., G. I. Papakostas, et al. (2014). **"S-adenosyl methionine (same) versus escitalopram and placebo in major depression rct: Efficacy and effects of histamine and carnitine as moderators of response."** *Journal of Affective Disorders* 164(0): 76-81. <http://www.sciencedirect.com/science/article/pii/S0165032714001529>

Abstract Objective To assess the antidepressant efficacy of S-adenosyl methionine (SAME), a naturally occurring methyl donor, versus the selective serotonin reuptake inhibitor (SSRI) escitalopram and a placebo control; and to determine whether serum histamine or carnitine levels modified treatment response. **Methods** We examined a subsample (n=144) from one site of a two-site study of adults with diagnosed Major Depressive Disorder (MDD), recruited from 4/13/05 to 12/22/09, who consented to the additional blood draw for serum histamine and carnitine levels. After washout, eligible subjects were randomized to SAME (1600–3200 mg/daily), escitalopram (10–20 mg/daily), or matching placebo for 12 weeks of double-blind treatment (titration at week 6 in non-response). **Results** On the primary outcome of the Hamilton Depression Rating Scale (HAM-D-17), a significant difference in improvement was observed between groups from baseline to week 12 (p=0.039). The effect size from baseline to endpoint was moderate to large for SAME versus placebo (d=0.74). SAME was superior to placebo from week 1, and to escitalopram during weeks 2, 4, and 6. No significant effect was found between escitalopram and placebo or SAME. Response rates (HAM-D-17≥50% reduction) at endpoint were 45%, 31%, and 26% for SAME, escitalopram, and placebo, respectively; while remission rates (HAM-D≤7) were 34% for SAME (p=0.003), 23% for escitalopram (p=0.023), and 6% for placebo. No correlation between baseline histamine level and reduction of HAM-D-17 score was found for either the SAME or escitalopram groups. Baseline carnitine levels were also not found to moderate response to either treatment. **Limitations** While SAME appears to be an effective antidepressant agent, the overall findings from the parent study (which showed no significant difference between groups due to site differences) must be taken into consideration. **Conclusions** These preliminary results provide encouraging evidence for the use of SAME in the treatment of MDD. Histamine and carnitine serum level may not necessarily moderate response to SAME.

Shahmansouri, N., M. Farokhnia, et al. (2014). **"A randomized, double-blind, clinical trial comparing the efficacy and safety of crocus sativus l. With fluoxetine for improving mild to moderate depression in post percutaneous coronary intervention patients."** *J Affect Disord* 155: 216-222. <http://www.ncbi.nlm.nih.gov/pubmed/24289892>

OBJECTIVE: A significant correlation exists between coronary artery diseases and depression. The aim of this trial was to compare the efficacy and safety of saffron versus fluoxetine in improving depressive symptoms of patients who were suffering from depression after performing percutaneous coronary intervention (PCI). **METHODS:** In this randomized double-blind parallel-group study, 40 patients with a diagnosis of mild to moderate depression who had undergone PCI in the last six months were randomized to receive either fluoxetine (40mg/day) or saffron (30mg/day) capsule for six weeks. Participants were evaluated by Hamilton depression rating scale (HDRS) at weeks 3 and 6 and the adverse events were systematically recorded. **RESULTS:** By the study endpoint, no significant difference was detected between two groups in reduction of HDRS scores (P=0.62). Remission and response rates were not significantly different as well (P=1.00 and P=0.67; respectively). There was no significant difference between two groups in the frequency of adverse events during this trial. **LIMITATIONS:** Relatively small sample size and short observational period were the major limitations of this study. **CONCLUSION:** Short-term therapy with saffron capsules showed the same antidepressant efficacy compared with fluoxetine in patients with a prior history of PCI who were suffering from depression.

Sharpe, M., J. Walker, et al. (2014). **"Integrated collaborative care for comorbid major depression in patients with cancer (smart oncology-2): A multicentre randomised controlled effectiveness trial."** *The Lancet* 384(9948): 1099-1108. <http://www.sciencedirect.com/science/article/pii/S0140673614612319>

Summary Background Medical conditions are often complicated by major depression, with consequent additional impairment of quality of life. We aimed to compare the effectiveness of an integrated treatment programme for major depression in patients with cancer (depression care for people with cancer) with usual care. **Methods** SMaRT Oncology-2 is a parallel-group, multicentre, randomised controlled effectiveness trial. We enrolled outpatients with major depression from three cancer centres and their associated clinics in Scotland, UK. Participants were randomly assigned in a 1:1 ratio to the depression care for people with cancer intervention or usual care, with stratification (by trial centre) and minimisation (by age, primary cancer, and sex) with allocation concealment. Depression care for people with cancer is a manualised, multicomponent collaborative care treatment that is delivered systematically by a team of cancer nurses and psychiatrists in collaboration with primary care physicians. Usual care is provided by primary care physicians. Outcome data were collected up until 48 weeks. The primary outcome was treatment response (≥50% reduction in Symptom Checklist Depression Scale [SCL-20] score, range 0–4) at 24 weeks. Trial statisticians and data collection staff were masked to treatment allocation, but participants could not be masked to the allocations. **Analyses** were by intention to treat. This trial is registered with Current Controlled Trials, number ISRCTN40568538. **Findings** 500 participants were enrolled between May 12, 2008, and May 13, 2011; 253 were randomly allocated to depression care for people with cancer and 247 to usual care. 143 (62%) of 231 participants in the depression care for people with cancer group and 40 (17%) of 231 in the usual care group responded to treatment: absolute difference 45% (95% CI 37–53), adjusted odds ratio 8.5 (95% CI 5.5–13.4), p<0.0001. Compared with patients in the usual care group, participants allocated to the depression care for people with cancer programme also had less depression, anxiety, pain, and fatigue; and better functioning, health, quality of life, and perceived quality of depression care at all timepoints (all p<0.05). During the study, 34 cancer-related deaths occurred (19 in the depression care for people with cancer group, 15 in the usual care group), one patient in the depression care for people with cancer group was admitted to a psychiatric ward, and one patient in this group attempted suicide. None of these events were judged to be related to the trial treatments or procedures. **Interpretation** Our findings suggest that depression care for people with cancer is an effective treatment for major depression in patients with cancer. It offers a model for the treatment of depression comorbid with other medical conditions.

Tsai, J., J. D. Elhai, et al. (2014). **"Comparing four competing models of depressive symptomatology: A confirmatory factor analytic study of 986,647 U.S. Veterans."** *Journal of Affective Disorders* 165(0): 166-169. <http://www.sciencedirect.com/science/article/pii/S0165032714002699>

Abstract Background Few rigorous studies have examined the factor structure of major depression symptoms as assessed by current diagnostic systems. This study evaluated four competing models of depressive symptomatology among a large, heterogeneous sample of U.S. veterans. **Methods** To determine the best fitting model of major depressive symptoms among four competing models, this study conducted a series of confirmatory factor analyses on a national sample of 986,647 U.S. veterans. **Results** A two-factor model first reported by Krause, Reed, and McArdle (2010) provided superior fit to symptom-level data compared to three other models. The optimal model consists of a somatic factor including anhedonia, sleep difficulties, fatigue, appetite changes, concentration difficulties, and psychomotor agitation; and a non-somatic factor including depressed mood, feelings of worthlessness, and thoughts of death. Factorial invariance testing found this model to be invariant

by gender and major depression diagnosis. Limitations A widely used self-report measure of depression was used and the sample consisted solely of veterans so further study is needed with clinician-administered measures and non-veteran samples. Conclusions Together, these findings support separating symptoms of major depression into somatic and non-somatic factors which may have clinical relevance, and help clarify debates about the factor structure of depressive symptoms.

Vashum, K. P., M. McEvoy, et al. (2014). **"Dietary zinc is associated with a lower incidence of depression: Findings from two Australian cohorts."** *Journal of Affective Disorders* 166(0): 249-257. <http://www.sciencedirect.com/science/article/pii/S0165032714003048>

Background Several animal and human studies have shown that zinc plays a role in reducing depression, but there have been no longitudinal studies in both men and women on this topic. The aim of this study was to investigate dietary zinc, and the zinc to iron ratio, as predictors of incident depression in two large longitudinal studies of mid-age and older Australians. **Methods** Data were self-reported, as part of the Australian Longitudinal Study on Women's Health (women aged 50–61 years) and Hunter Community Study (men and women aged 55–85 years). Validated food frequency questionnaires were used to assess dietary intake. Energy-adjusted zinc was ranked using quintiles and predictors of incident depression were examined using multivariate logistic regression. **Results** Both studies showed an inverse association between dietary zinc intake and risk of depression, even after adjusting for potential confounders. Compared to those with the lowest zinc intake those with the highest zinc intake had significantly lower odds of developing depression with a reduction of about 30–50%. There was no association between the zinc to iron ratio and developing depression in either study. **Limitations** Dietary assessment was carried out only at baseline and although adjustments were made for all known potential confounders, residual confounding cannot be entirely excluded. **Conclusions** Low dietary zinc intake is associated with a greater incidence of depression in both men and women, as shown in two prospective cohorts. Further studies into the precise role of zinc compared to other important nutrients from the diet are needed.

Walker, J., C. H. Hansen, et al. (2014). **"Integrated collaborative care for major depression comorbid with a poor prognosis cancer (smart oncology-3): A multicentre randomised controlled trial in patients with lung cancer."** *The Lancet Oncology* 15(10): 1168-1176. <http://www.sciencedirect.com/science/article/pii/S1470204514703432>

Background The management of depression in patients with poor prognosis cancers, such as lung cancer, creates specific challenges. We aimed to assess the efficacy of an integrated treatment programme for major depression in patients with lung cancer compared with usual care. **Methods** Symptom Management Research Trials (SMaRT) Oncology-3 is a parallel-group, multicentre, randomised controlled trial. We enrolled patients with lung cancer and major depression from three cancer centres and their associated clinics in Scotland, UK. Participants were randomly assigned in a 1:1 ratio to the depression care for people with lung cancer treatment programme or usual care by a database software algorithm that used stratification (by trial centre) and minimisation (by age, sex, and cancer type) with allocation concealment. Depression care for people with lung cancer is a manualised, multicomponent collaborative care treatment that is systematically delivered by a team of cancer nurses and psychiatrists in collaboration with primary care physicians. Usual care is provided by primary care physicians. The primary outcome was depression severity (on the Symptom Checklist Depression Scale [SCL-20], range 0–4) averaged over the patient's time in the trial (up to a maximum of 32 weeks). Trial statisticians and data collection staff were masked to treatment allocation, but patients and clinicians could not be masked to the allocations. Analyses were by intention to treat. This trial is registered with Current Controlled Trials, number ISRCTN75905964. **Findings** 142 participants were recruited between Jan 5, 2009, and Sept 9, 2011; 68 were randomly allocated to depression care for people with lung cancer and 74 to usual care. 43 (30%) of 142 patients had died by 32 weeks, all of which were cancer-related deaths. No intervention-related serious adverse events occurred. 131 (92%) of 142 patients provided outcome data (59 in the depression care for people with lung cancer group and 72 in the usual care group) and were included in the intention-to-treat primary analysis. Average depression severity was significantly lower in patients allocated to depression care for people with lung cancer (mean score on the SCL-20 1.24 [SD 0.64]) than in those allocated to usual care (mean score 1.61 [SD 0.58]); difference -0.38 (95% CI -0.58 to -0.18); standardised mean difference -0.62 (95% CI -0.94 to -0.29). Self-rated depression improvement, anxiety, quality of life, role functioning, perceived quality of care, and proportion of patients achieving a 12-week treatment response were also significantly better in the depression care for people with lung cancer group than in the usual care group. **Interpretation** Our findings suggest that major depression can be treated effectively in patients with a poor prognosis cancer; integrated depression care for people with lung cancer was substantially more efficacious than was usual care. Larger trials are now needed to estimate the effectiveness and cost-effectiveness of this care programme in this patient population, and further adaptation of the treatment will be necessary to address the unmet needs of patients with major depression and even shorter life expectancy. Funding Cancer Research UK and Chief Scientist Office of the Scottish Government.

Walker, J., C. H. Hansen, et al. (2014). **"Prevalence, associations, and adequacy of treatment of major depression in patients with cancer: A cross-sectional analysis of routinely collected clinical data."** *The Lancet Psychiatry* 1(5): 343-350. <http://www.sciencedirect.com/science/article/pii/S221503661470313X>

Summary Background Major depression is an important complication of cancer. However, reliable data are lacking for the prevalence of depression in patients with cancer in different primary sites, the association of depression with demographic and clinical variables within cancer groupings, and the proportion of depressed patients with cancer receiving potentially effective treatment for depression. We investigated these questions with data from a large representative clinical sample. **Methods** We analysed data from patients with breast, lung, colorectal, genitourinary, or gynaecological cancer who had participated in routine screening for depression in cancer clinics in Scotland, UK between May 12, 2008, and Aug 24, 2011. Depression screening was done in two stages (first, Hospital Anxiety and Depression Scale; then, major depression section of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition). Data for depression status were linked with demographic and clinical data obtained from the Scottish National Cancer Registry. **Findings** We analysed data for 21 151 patients. The prevalence of major depression was highest in patients with lung cancer (13.1%, 95% CI 11.9–14.2%), followed by gynaecological cancer (10.9%, 9.8–12.1), breast cancer (9.3%, 8.7–10.0), colorectal cancer (7.0%, 6.1–8.0), and genitourinary cancer (5.6%, 4.5–6.7). Within these cancer groupings, a diagnosis of major depression was more likely in patients who were younger, had worse social deprivation scores, and, for lung cancer and colorectal cancer, female patients. 1130 (73%) of 1538 patients with depression and complete patient-reported treatment data were not receiving potentially effective treatment. **Interpretation** Major depression is common in patients attending cancer clinics and most goes untreated. A pressing need exists to improve the management of major depression for patients attending specialist cancer services. Funding Cancer Research UK and Chief Scientist Office of the Scottish Government.

Wardenaar, K. J., H. J. Conradi, et al. (2014). **"Personality modulates the efficacy of treatment in patients with major depressive disorder."** *J Clin Psychiatry* 75(9): e916-923. <http://www.ncbi.nlm.nih.gov/pubmed/25295434>

OBJECTIVE: Effects of depression treatment are obscured by heterogeneity among patients. Personality types could be one source of heterogeneity that explains variability in treatment response. Clinically meaningful variations in personality

patterns could be captured with data-driven subgroups. The aim of this study was to identify such personality types and to explore their predictive value for treatment efficacy. **METHOD:** Participants (N = 146) in the current exploratory study came from a randomized controlled trial in primary care depressed patients, conducted between January 1998 and June 2003, comparing different treatments. All participants were diagnosed with a major depressive disorder (MDD) according to the DSM-IV. Primary (care as usual [CAU] or CAU plus a psychoeducational prevention program [PEP]) and specialized (CAU + PEP + psychiatric consultation or cognitive-behavioral therapy) treatment were compared. Personality was assessed with the Neuroticism-Extraversion-Openness Five-Factor Inventory (NEO-FFI). Personality classes were identified with latent profile analysis (LPA). During 1 year, weekly depression ratings were obtained by trimonthly assessment with the Composite International Diagnostic Interview. Mixed models were used to analyze the effects of personality on treatment efficacy. **RESULTS:** A 2-class LPA solution fit best to the NEO-FFI data: Class 1 (vulnerable, n = 94) was characterized by high neuroticism, low extraversion, and low conscientiousness, and Class 2 (resilient, n = 52) by medium neuroticism and extraversion and higher agreeableness and conscientiousness. Recovery was quicker in the resilient class (class x time: $P < .001$). Importantly, specialized treatment had added value only in the vulnerable class, in which it was associated with quicker recovery than primary treatment (class x time x treatment: $P < .001$). **CONCLUSIONS:** Personality profile may predict whether specialized clinical efforts have added value, showing potential implications for planning of treatments.

Wiersma, J. E., D. J. F. Van Schaik, et al. (2014). **"The effectiveness of the cognitive behavioral analysis system of psychotherapy for chronic depression: A randomized controlled trial."** *Psychotherapy and Psychosomatics* 83(5): 263-269. <http://www.karger.com/DOI/10.1159/000360795>

It is widely agreed that chronic depression is difficult to treat, knowledge about optimal treatment approaches is emerging. A multisite randomized controlled trial was conducted comparing the cognitive behavioral analysis system of psychotherapy (CBASP), a psychotherapy model developed specifically to treat chronic depression (n = 67) with care as usual (CAU; evidence-based treatments, n = 72) over a period of 52 weeks, with 23 sessions on average, in 3 outpatient clinics in the Netherlands. In both arms algorithm-based pharmacotherapy was provided. Patients (aged 18-65) met criteria for a DSM-IV diagnosis of major depressive disorder with diagnostic specifiers (chronic, without interepisode recovery) or with co-occurring dysthymic disorder indicating a chronic course. The Inventory for Depressive Symptomatology (IDS) Self-Report was used as the primary outcome measure. Mixed-effects linear regression analysis was used to compare the changes on the IDS scores between CBASP and CAU. The IDS was administered before treatment, and after 8, 16, 32 and 52 weeks. Results: At week 52, patients assigned to CBASP had a greater reduction of depressive symptoms compared to patients assigned to CAU ($t = -2.00$, $p = 0.05$). However, CBASP and CAU did not differ from each other on the IDS after 8 weeks ($t = 0.49$, $p = 0.63$), 16 weeks ($t = -0.03$, $p = 0.98$) and 32 weeks ($t = -0.17$, $p = 0.86$) of treatment. Conclusions: This trial shows that CBASP is at least as effective as standard evidence-based treatments for chronic depression. In the long run, CBASP appears to have an added effect.